

CASE REPORTS

◀ Primary Systemic Amyloidosis ◀ Violent Reaction to Phenolphthalein

Primary Systemic Amyloidosis

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PRIMARY systemic amyloidosis is a well-defined but infrequently observed disease. Since fewer than 50 cases have been reported^{1,2} to date, and the difficulties in arriving at a correct diagnosis are enhanced by variation in location of the amyloid deposit,³ an attempt at further correlation of clinical and pathological findings seems warranted.

CASE REPORT

Clinical History: A 54-year-old white male entered the hospital on March 22, 1947, as a transfer from a Naval hospital where he had been since August, 1946. The patient had been in good health, working as an automobile mechanic, up to January, 1946, when he had an acute illness characterized by fever, generalized aches and pains, and shortness of breath. He was hospitalized for one month and the illness was supposedly diagnosed as "flu." He returned to work and remained in good health until August 1946 when epigastric pain, nausea, and vomiting developed. A gastro-intestinal roentgenogram at the Naval hospital was reported as showing duodenal irritability. On a Sippy regimen, the patient improved and subsequent gastro-intestinal roentgenograms were normal. In September 1946 shooting pains in both arms and legs developed with a superficial burning sensation in the hands and feet. Progressive muscle weakness in all four extremities was noted, with pronounced edema of the legs, and the patient complained of frequency of urination. The blood pressure was low and electrocardiograms showed low voltage with inversion of T waves. Results of Wassermann test of the spinal fluid were questionably positive on one occasion and negative on repeat examination. The spinal fluid protein content was 60 mg. per 100 cc. and the colloidal gold curve was negative. Considered to have syphilis of the central nervous system, the patient was given a course of penicillin and then transferred to this hospital.

The past history was essentially negative. Syphilis was denied.

Physical Examination: On admission the patient appeared to be undernourished and chronically ill. The skin and mucous membranes were pale. There was no lymphadenopathy. The pupils were irregular, dilated, did not react to light but did react to accommodation. The cranial nerves were otherwise intact. The heart was not enlarged to percussion. On admission the heart sounds were inaudible to all examiners. Blood pressure was 82 mm. of mercury systolic and 64 mm. diastolic. Subsequently the heart sounds could be heard but were very faint. The rhythm was regular. The lungs were clear. There was some tenderness in the right

upper quadrant of the abdomen, but no organs were felt. There was pronounced atrophy of all the muscle groups in all four extremities. There was almost complete loss of muscle power in both lower extremities and at least 50 per cent loss in both upper extremities. Fibrillary twitchings were visible. There was a "glove and stocking" type of hypesthesia present. All deep reflexes were absent. There were no pathological reflexes. Position sense and vibratory sense were intact. There was marked pitting edema in both lower extremities.

Laboratory Examinations: Examination of the blood revealed the following: Hemoglobin 10.7 gm. per 100 cc.; erythrocytes 3.75 million; leukocytes 6,900 with normal differential; mean corpuscular volume 88 cubic microns; mean corpuscular hemoglobin 30 micromicrograms; mean corpuscular hemoglobin concentration 33 per cent. Blood proteins: Albumin, 2.63 gm. per 100 cc.; globulin, 2.99 gm. per 100 cc.; albumin-globulin ratio, 0.88:1. The Kahn test was negative. The urine contained a heavy trace of albumin with occasional hyaline casts and rare erythrocytes. The specific gravity was fixed at a low level. The phenolsulfonephthalein test showed 15 per cent excretion in two hours. The average 24-hour urinary albumin was 5.0 gm. Blood urea was 33 mg. per 100 cc.

Gastric analysis showed a normal free and total acidity. Roentgenograms of the entire gastro-intestinal tract showed no abnormality. Excretory urograms showed poor dye excretion, but no other abnormality. An x-ray film of the chest revealed no abnormality, and fluoroscopy of the heart revealed a normal cardiac outline with normal pulsations.

The electrocardiograms showed a rate of 75; sinus rhythm; PR interval 0.2 second; QRS interval 0.08 second; there was low voltage of all the QRS complexes, and the T waves were flattened in all leads.

Course: It was felt that the patient did not have central nervous system syphilis, and a diagnosis of Guillain-Barré syndrome was considered. Physiotherapy was given but resulted in little improvement of muscle power. Because of the low blood pressure, inaudible heart sounds and electrocardiographic findings, pericarditis with effusion was considered until cardiac fluoroscopy ruled it out. The circulation time with Decholin was 20 seconds. The patient was digitalized with only slight improvement.

The anemia was progressive, the erythrocyte count dropping to 2.87 million and the hemoglobin to 7.2 gm. per 100 cc. Liver and iron therapy and repeated blood transfusions brought no improvement.

An attempt was made to correct the hypoproteinemia with repeated plasma transfusions, but this also was unsuccessful.

The patient complained periodically of epigastric pain, nausea and vomiting. Constipation was persistent. During the last two months of life the patient complained of dryness of the mouth and thickness of the tongue. Visible enlargement of the tongue was noted. Dysphonia and dysphagia developed and became progressively more severe. In the last month of life urinary retention developed and catheteriza-

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tion was necessary. It was the opinion of the genito-urinary consultant that this was due to the primary neurological disease. Death occurred suddenly on November 21, 1947.

Necropsy Findings: Autopsy was performed 15 hours after death. The skin was pale, turgid, and free of lesions. The tongue was large and coated. The abdominal cavity contained 500 ml. and the pleural spaces each 300 ml. of cloudy yellow fluid. The lungs grossly were intact. The heart was large and weighed 620 gm. The right and left ventricular walls contributed equally to the increase in size, measuring 10 and 12 mm. respectively. The cut surface of the heart muscle was of brown red, uniformly waxy appearance. The spleen weighed 540 gm. It showed a smooth dark purple, diffusely waxy surface. The malpighian corpuscles could not be made out. The liver weighed 2,700 gm. Its edges were rounded. The lobular architecture was well preserved. Although kidneys were not enlarged, the cortex was narrow and of yellowish color with the architecture blurred, and numerous indented scars were present on the surface. The iodine test for amyloid carried out on heart, spleen, liver, and kidneys was negative. The other organs were grossly free of lesions save for arteriosclerotic changes of the aorta and of the vessels at the base of the brain.

Lungs: The media of several small vessels was partly replaced by an amorphous homogeneously pink-staining material.

Heart: The fibrillary structure was in many places poorly preserved or not visible at all. In many instances, the muscle fibres were spread apart or surrounded, sometimes compressed by irregularly arranged waxy pink-staining fibres. In places, similarly staining globules replaced muscle fibres partly or entirely. An identical material was seen in many branches of the coronary vessels, replacing largely the media. Fine pink fibres enlarged also the subintimal space narrowing the lumen. Congo red stained only the material in the vascular walls. In a Masson stain the acellular fibres took up various hues of green. Sudan IV stains of frozen sections revealed no lipid material.

Spleen: The reticulum was widened by a deposit of pink-staining material compressing the sinusoids and reducing the malpighian corpuscles to small groups of lymphocytes. The deposit stained bright brown red with Congo red, but not with Sudan IV in frozen sections.

Liver: Many of the vessels except some central veins showed deposits as described.

Adrenal glands and pancreas: The vessel walls as well as the neurilemma of sympathetic nerve branches were the seat of amyloid deposit. There was increase in width of the zona glomerulosa of the adrenal without alteration of the character of the cells. Cells of the surrounding fatty tissue showed thickening of the cellular membrane by homogeneously pink-staining material which was identified as amyloid by a positive Congo red stain.

Kidneys: Amyloid deposit as seen in secondary amyloidosis was noted in the glomerular loops as well as in the wall of small vessels. These deposits reacted positively with Congo red.

Intestine and bladder: The vessels showed changes similar to those of the adrenal glands.

Skin: There was no evidence of amyloid change.

Brain and spinal cord: Some of the meningeal vessels were affected as described for lungs and liver, but the parenchyma was free of amyloid deposit. Amylaceous bodies were frequently noted and were particularly numerous in the parenchyma surrounding the third ventricle.

COMMENT

This case of amyloidosis presents many of the features which are characteristic of the primary form of the disease: (1) No specific etiological factor was present; (2) although

amyloid deposits were present in spleen and kidneys, as is common with secondary amyloidosis, the deposit in the heart, sympathetic ganglia and blood vessels of the liver, pancreas, adrenal, intestine, bladder, and meninges is typical of the primary form; (3) staining reactions were atypical.

The most striking clinical feature was the degree of neuromuscular involvement. Unfortunately sections of skeletal muscle and peripheral nerves were not taken, but pronounced weakness, muscular atrophy and areflexia have been reported and explained on the basis of amyloid deposit in skeletal muscle or peripheral nerves.⁷ The pupillary findings, early gastro-intestinal symptoms, and urinary retention may be due to involvement of the autonomic nervous system.

Of considerable interest in this case were the cardiovascular findings. The poor quality of the heart sounds, the low blood pressure, and, in part, the dyspnea and edema may be explained by the amyloid infiltration both in the myocardium and in the smaller cardiac vessels. The electrocardiographic pattern of low voltage and flattened T waves is considered to be typical and results from alteration of conduction through the abnormal myocardium.

Enlargement of the tongue associated with dysphagia and dysphonia, all of which were present in the case, are frequent findings in primary amyloidosis, due to infiltration of the tongue, buccal mucosa, larynx and trachea.^{4,8}

Abdominal pain, simulating that of peptic ulcer, and constipation were prominent symptoms. Amyloid infiltration of the gastroenteric tract may account for such symptoms,⁵ but was not found in this case. The symptoms may be explained on the basis of involvement of the autonomic nervous system.

Mild anemia, of a normochromic, normocytic type, was a feature in this case. Pathologically there was considerable fatty tissue in the bone marrow, and the blood vessels of the marrow did contain amyloid, but erythropoiesis within the small groups of bone marrow cells appeared normal.

Kidney involvement is more common in secondary amyloidosis, but has also been described in the primary form.^{1,4} As illustrated here, the laboratory findings are: albuminuria, casts, disturbance of power of concentration, lowering of the serum protein, reversal of the albumin-globulin ratio, and retention of the waste products of metabolism in the final stage.

SUMMARY

A case of primary amyloidosis is reported. Attention is called to the clinical symptoms of this disease entity with its involvement of the heart, spleen, kidneys, nerves, skeletal muscle, and blood vessels of most of the remaining organs of the body.

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